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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/660,775	09/12/2003	Raymond J.H. Westheim	SYN-0032	5762

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EXAMINER

SHIAO, REI TSANG

ART UNIT	PAPER NUMBER
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1626

DATE MAILED: 06/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/660,775

Applicant(s)

WESTHEIM, RAYMOND J.H.

Examiner

Robert Shiao

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on responses filed on 05/04, 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) 23-29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12 September 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>01/14/2004</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This application claims benefit of the provisional application:
60/413,765 with a filing date 09/27/2002; and
60/470,223 with a filing date 05/14/2003.
2. Claims 1-29 are pending in the application.

Responses to Election/Restriction

3. Applicant's election with traverse of Group I claims 1-10, 14-22 in the reply filed on May 04, 2005, is acknowledged. The traversal is on the grounds that the Examiner has failed to establish that the six groups of claims are independent or that a serious burden would be imposed by search and examination. This is found persuasive, in part, and the reasons are given, *infra*.

Status of the Claims

4. Claims 1-29 are pending in the application. The scope of the invention of the elected subject matter is as follows:

Claims 1-22, drawn to a crystalline or amorphous forms of compound/ compositions of bicalutamide, classified in class 514/564 with various subclasses.

Groups I-II and III-VI are distinct and independent products, methods of use, and processes of making, one from the other on the basis of structure defined in the claimed products as directed to various forms (i.e., crystalline or amorphous forms) of compound bicalutamide, and they differ in elements, starting materials, dose, administration, bonding arrangement and chemical property to such an extent that a reference

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anticipating compounds of any one group would not render another group obvious.

Moreover, the examiner must perform a commercial database search on the subject matter of each group in addition to a paper search, which is quite burdensome to the examiner. Claims 1-22 are prosecuted in the case. Claims 23-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

The requirement is still deemed proper and is therefore made **FINAL**.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter “a crystalline bicalutamide of form II” or “a bicalutamide in amorphous form” without limitation, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, see claim 1 or 12, line 1, respectively.

6. Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the instant a crystalline bicalutamide of form II

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having x-ray diffraction peak at 25.9° , does not reasonably provide enablement for a crystalline bicalutamide of form II having x-ray diffraction peak at 40° . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

For rejections under 35 U.S.C. 112, first paragraph, the following factors must be considered (In re Wands, 8 USPQ2d 1400, 1988):

- 1) Nature of invention.
- 2) State of prior art.
- 3) Level of ordinary skill in the art.
- 4) Level of predictability in the art.
- 5) Amount of direction and guidance provided by the inventor.
- 6) Existence of working examples.
- 7) Breadth of claims.
- 8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See below:

1) Nature of the invention

The claims are drawn to a crystalline bicalutamide of form II or an amorphous form of bicalutamide without limitation.

2) State of the prior art

The reference Gray's US 5,985,868 does not indicate which compounds of instant compounds may be useful in the claimed invention. Gray's '868 is pertaining to

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method and compositions for treating androgen-dependent disease using optically pure R-(-) casodex.

3) Level of ordinary skill in the art.

The level of ordinary skill in the art is high. The claims are drawn to a crystalline bicalutamide of form II or an amorphous form of bicalutamide without limitation by the instant examples disclosed in the specification.

4) Level of predictability in the art.

The claims are drawn to a crystalline bicalutamide of form II or an amorphous form of bicalutamide without limitation, there would be little predictability in the scope of claimed products.

5) Amount of direction and guidance provided by the inventor.

The claims are drawn to a crystalline bicalutamide of form II or an amorphous form of bicalutamide without limitation, i.e., a crystalline bicalutamide of form II having x-ray diffraction peak at 40° , which are neither enabled nor supported in the specification.

6) Existence of working examples.

The claims are drawn to a crystalline bicalutamide of form II or an amorphous form of bicalutamide without limitation, encompasses a vast number of products. Applicant's limited working examples do not enable the public to use such a numerous amount of "a crystalline bicalutamide of form II or an amorphous form of bicalutamide without limitation" in the specification. Applicants claim "a crystalline bicalutamide of

form II or an amorphous form of bicalutamide without limitation", however, the specification provides only limited examples of products.

7) Breadth of claims.

The claims are extremely broad due to the vast number of possible "a crystalline bicalutamide of form II or an amorphous form of bicalutamide without limitation".

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The specification did not enable any person skilled in the art to which it pertains to make or use the invention commensurate in scope with the claims. In particular, the specification failed to enable the skilled artisan to practice the invention without undue experimentation. The skilled artisan would have a numerous products in order to obtain "a crystalline bicalutamide of form II or an amorphous form of bicalutamide without limitation" as claimed. Based on the unpredictable nature of the invention and state of the prior art and the extreme breadth of the claims, one skilled in the art could not perform the claimed compounds without undue experimentation, see *In re Armbruster* 185 USPQ 152 CCPA 1975. Incorporation of the limitation "a crystalline bicalutamide of form II or an amorphous form of bicalutamide without limitation" would obviate the rejection, i.e., X-ray diffraction data, see pages 14-18 of the specification.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 8, and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 or 8, line 2, recites the limitation "figure 4" or "figure 2", fails to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims must stand alone to define invention, and incorporation into claims by express reference to specification is not permitted, are properly rejected under 35 U.S.C. 112, second paragraph, see *Ex parte Fressola*, No. 93-0828. Incorporation of the IR absorbance spectra of figure 4 or X-ray diffractogram data into the claims respectively would obviate the objection.

Claim 11, recites limitation "crystalline bicalutamide", fails to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear which crystalline form of bicalutamide is. Is it form II or form I of crystalline bicalutamide? Clarification is required, see page 2, line 18.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-11 and 14-22 are rejected under 35 U.S.C. 102(a) as being anticipated by Ekwuribe's US 6,583,306. Ekwuribe's '306 is 102 (e) reference.

Applicants claim a crystalline bicalutamide and its pharmaceutical compositions. The instant crystalline bicalutamide has been found on the page 1-18 of the specification.

Ekwuribe's '306 disclose a compound N-(4-cyano-3-trifluoromethyl-phenyl)-3-(4-fluoro-phenylsulfonyl)-2-hydroxy-2-methyl-propionamide (i.e., bicalutamide) in white crystal form, which clearly anticipate instant crystalline bicalutamide (i.e., form II), see column 16, Example 5, lines 35-48.

Claims 13-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Tucker's US 4,636,505.

Tucker's '505 disclose a pharmaceutical compositions (i.e., oral dosage or solution) comprising a compound 4-cyano-3-trifluoromethyl-phenyl-N-(3-p-fluorophenylsulfonyl)-2-hydroxy-2-methyl-propionyl)aniline (i.e., bicalutamide in crystalline form), which clearly anticipate the instant compositions comprising crystalline bicalutamide, see column 18, lines 9-22, and column 15, lines 1-6.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

"Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re

Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Also see M.P.E.P. 2113.

10. Claims 1-11 and 14-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ekwuribe's US 6,583,306.

Applicants claim a crystalline bicalutamide and its pharmaceutical compositions as agents producing antiandrogenic effect. The instant crystalline bicalutamide has been found on the page 1-18 of the specification.

Determination of the scope and content of the prior art (MPEP §2141.01)

Ekwuribe's '306 disclose a compound N-(4-cyano-3-trifluoromethyl-phenyl)-3-(4-fluoro-phenylsulfonyl)-2-hydroxy-2-methyl-propionamide (i.e., bicalutamide) as agents (i.e., pharmaceutical composition) treating prostate cancer, Ekwuribe's compound bicalutamide is in white crystal form, see column 1, lines 19-26, and column 16, Example 5, lines 35-48.

Determination of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and Ekwuribe's is that Ekwuribe silence the instant crystalline form II or I.

Finding of prima facie obviousness-rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art would find the claims 1-11 and 14-22 prima facie obvious because one would be motivated to employ the crystalline form of

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Ekwuribe's compound bicalutamide to obtain instant bicalutamide in crystalline forms (i.e., form II or I) and their pharmaceutical compositions.

The motivation to make the claimed compounds derives from the expectation that the instant claimed bicalutamide in crystalline forms and their pharmaceutical compositions would possess similar activities, i.e., producing antiandrogenic effect or treating prostate cancer, from the known Ekwuribe's compounds to that which is claimed in the reference.

The instant crystalline form of bicalutamide is obvious from the crystalline form disclosed by Ekwuribe absent a showing of unexpected result. To demonstrate unobviousness, applicants must show unexpected result stemming from the instant crystalline form over the crystalline form of Ekwuribe's in form of mechanical advantage(s) of the instant crystal over the crystal of Ekwuribe's, see *Ex parte Conn and Norman*, 119 USPQ 388 (1956), also see *In re Grose & Flanigen*, 201 USPQ57.

11. Claims 1-11 and 14-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tucker's US 4,636,505.

Applicants claim a crystalline bicalutamide and its pharmaceutical compositions as agents producing antiandrogenic effect. The instant crystalline bicalutamide has been found on the page 1-18 of the specification.

Determination of the scope and content of the prior art (MPEP §2141.01)

Tucker's '505 disclose a compound 4-cyano-3-trifluoromethyl-phenyl-N-(3-p-fluorophenylsulfonyl-2-hydroxy-2-methyl-propionyl)aniline (i.e., bicalutamide in crystalline form) and its pharmaceutical compositions (i.e., oral dosage or solution), see column 18, lines 9-22, column 14, line 18, and column 15, lines 1-6. Tucker's compound/compositions of bicalutamide is used for antiandrogenic effect, see column 18, 28-31.

Determination of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and Tucker's is that Tucker's silence the instant crystalline form II or I.

Finding of prima facie obviousness-rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art would find the claims 1-11 and 14-22 prima facie obvious because one would be motivated to employ the crystalline form of Tucker's compound bicalutamide to obtain instant bicalutamide in crystalline forms (i.e., form II or I) and their pharmaceutical compositions.

The motivation to make the claimed compounds derives from the expectation that the instant claimed bicalutamide in crystalline forms and their pharmaceutical compositions would possess similar activities, i.e., producing antiandrogenic effect or treating prostate cancer, from the known Tucker's compounds to that which is claimed in the reference.

The instant crystalline form of bicalutamide is obvious from the crystalline form disclosed by Tucker absent a showing of unexpected result. To demonstrate unobviousness, applicants must show unexpected result stemming from the instant crystalline form over the crystalline form of Tucker's in form of mechanical advantage(s) of the instant crystal over the crystal of Tucker's, see *Ex parte Conn* and *Norman*, 119 USPQ 388 (1956), also see *In re Grose & Flanigen*, 201 USPQ57.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 13-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 or 11 of Ortega et al. co-pending application No. 10/842,632 see US 2005/000,8691 A1. Although the conflicting claims are not identical, they are not patentably distinct from each other and reasons are as follows.

Applicants claim a pharmaceutical composition (i.e., an oral dosage form) comprising a compound bicalutamide (i.e., in crystalline and/or amorphous forms) and a pharmaceutical acceptable excipient. The pharmaceutical compositions are found on the pages 1-18 of the specification.

Ortega et al. claim a pharmaceutical compositions (i.e., a granulate in an oral dosage form) comprising a compound bicalutamide (i.e., at least 50% bicalutamide) and one pharmaceutical acceptable excipient.

The difference between the instant claims and Ortega et al. is that the instant claims silence the granulate form (i.e., solid form) of Ortega et al.

One having ordinary skill in the art would find the claims 13-22 prima facie obvious because one would be motivated to employ the pharmaceutical compositions of Ortega et al. to obtain instant pharmaceutical compositions, wherein the instant compositions (i.e., solid, or solid oral dosage form) comprise bicalutamide and a

pharmaceutical acceptable excipient.

The motivation to make the claimed compounds derives from the expectation that the instant claimed pharmaceutical compositions would possess similar activities, i.e., producing antiandrogenic effect or treating prostate cancer, from the known Ortega et al. pharmaceutical compositions to that which is claimed in the reference.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Shiao whose telephone number is (571) 272-0707. The examiner can normally be reached on 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.


Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

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you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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June 13, 2005